No potential conflict of interest relevant to this letter was reported.

1. Zhao D, Liu J, Wang W, et al. Epidemiological transition of stroke in China: twenty-one-year observational study from the Sino-MONICA-Beijing Project. Stroke 2008;39:1668-74.
2. Turin TC, Kokubo Y, Murakami Y, et al. Lifetime risk of stroke in Japan. Stroke 2010;41:1552-4.
3. Wang W, Jiang B, Sun H, et al. Prevalence, incidence, and mortality of stroke in China: results from a nationwide population-based survey of 480 687 adults. Circulation 2017;135:759-71.

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THE AUTHORS REPLY: In response to Liu et al.: there are three reasons why we included all age groups in our analysis. First, we produced comparable risk estimates for all countries, including those with populations that had a sex-specific life expectancy close to or greater than 85 years. Second, we accounted for competing risks of death and total survival up to any age by multiplying the age-specific probability of having a stroke by the probability of surviving to that age without having a stroke. Third, we intended to capture the risks of stroke throughout a person's lifespan rather than only up to an arbitrary age limit. For these reasons, we believe that it is reasonable to not place an upper age restriction on the lifetime risk metric.

In response to Zhao and Huang: we reported that the lifetime risk of stroke in China was higher among men than among women, consistent with the commenters' assertions. However the estimates of lifetime risk of stroke were based on the stroke incidence, prevalence, and mortality (including competing risk of death) that were estimated in the GBD study and not on the respective rates as observed in a specific cohort.[1,2] We reported that the lifetime risk of stroke in Japan was slightly higher among women (23.6%) than among men (22.5%), although the uncertainty intervals for these two groups overlapped, which is consistent with the findings from a previous study on lifetime risk of stroke in Japan.[3] The results from the GBD 2016 study are similar to those previously reported in Japan, even though our lifetime risks were generated with the use of estimates of stroke incidence and mortality among persons older than 25 years in 2016 in order to calculate a period metric of lifetime risk, as opposed to the Japanese study in which a cohort metric based on estimates from 1989 through 2005 was used.[4] One contributing factor to the higher lifetime risk of stroke among women is the higher competing risk of death among men (life expectancy of 80.8 years among men in 2016) than among women (life expectancy of 86.9 years), which decreases the proportion of men who survive to older ages, when the risk of stroke is highest.[5]

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Since publication of their article, the authors report no further potential conflict of interest.

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Glucocorticoid-Induced Osteoporosis

TO THE EDITOR: We agree with Buckley and Humphrey (Dec. 27 issue)[1] that bisphosphonates are the drug of choice for the treatment of glucocorticoid-induced osteoporosis, but we believe that denosumab presents more shortcomings than advantages. In patients who receive treatment with glucocorticoids, the risk of fracture decreases rapidly when glucocorticoids are discontinued (and discontinuation is possible in many patients), but several studies have shown that the withdrawal of denosumab produces a rebound effect, with an abrupt decrease in bone

mineral density to values lower than the initial values and new vertebral fractures in 26% of patients.[2-5] Therefore, we disagree with the use of denosumab in the treatment of glucocorticoid-induced osteoporosis.

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No potential conflict of interest relevant to this letter was reported.

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THE AUTHORS REPLY: Sosa and Gómez de Tejada have concerns that the use of denosumab in the prevention or treatment of glucocorticoid-induced osteoporosis is detrimental owing to the rapid loss of bone mineral density and the increased risk of vertebral fracture in postmenopausal women when the drug is discontinued.[1,2] The risk of vertebral fracture in postmenopausal women 12 months after denosumab discontinuation is similar to that among postmenopausal women who did not receive the drug.[1] Risk is highest for patients with a history of vertebral fracture that was sustained before or during receipt of the drug.[1,3] Studies are required to determine whether discontinuation also increases the risk of vertebral fracture in patients treated with denosumab for the prevention or treatment of glucocorticoid-induced osteoporosis. Clinicians may opt to avoid denosumab in patients at high risk for vertebral fracture. We agree with the 2017 American College of Rheumatology guidelines on the use of denosumab in patients with glucocorticoid-induced osteoporosis, which recommend its use as a third-line treatment if patients cannot receive bisphosphonates or parathyroid hormone analogues.[4] On the basis of available data that suggest — but do not prove — that bisphosphonates may prevent excessive bone loss after denosumab discontinuation, clinicians may opt to transition these patients to another osteoporosis therapy when denosumab is discontinued.[5]

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Understanding Links among Opioid Use, Overdose, and Suicide

TO THE EDITOR: Bohnert and Ilgen (Jan. 3 issue)[1] provide a thoughtful perspective on opioid-related suicides. They describe "Deaths of Despair,"[2] an epidemiologic concept that warrants further root-cause analysis, particularly in geographic areas that are disproportionately affected by the opioid crisis.

The current boom–bust era of the coal industry has contributed to the uncertain welfare of the Appalachian population.[3] At the same time,